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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/655,570	09/04/2003	Danny Allen	MUR-005	6430

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EXAMINER	
BOWMAN, AMY HUDSON	

ART UNIT	PAPER NUMBER
1635	

DATE MAILED: 08/12/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/655,570	ALLEN ET AL.	
	Examiner.	Art Unit	
	Amy H. Bowman	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *27 July 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,18,20,23,24,26,28 and 31* is/are pending in the application.

4a) Of the above claim(s) *23,24,26 and 31* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1, 18, 20, and 28* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *04 September 2003* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Applicant's election of group I, claims 1, 18, 20 and 28, in the reply filed on 7/27/2005 is acknowledged. Although applicant's election appears to be with traverse, applicant has not provided any arguments.

Therefore, the requirement for restriction is still deemed proper and is therefore made FINAL.

Claims 23, 24, 26 and 31 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to nonelected inventions, there being no allowable generic or linking claim.

Sequence Compliance

This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 CFR 1.821 through 1.825 because there are sequences in figure 4 that do not contain a SEQ ID NO.

A complete response to this office action must correct the defects cited above regarding compliance with the sequence rules and a response to the action on the merits which follows.

The aforementioned instance of failure to comply is not intended as an exhaustive list of all such potential failures to comply in the instant application. Applicants are encouraged to thoroughly review the application to ensure that the entire

application is in full compliance with all sequence rules. This requirement will not be held in abeyance.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1, 18, 20 and 28 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Applicant has claimed "RNAi" as a compound. Throughout the instant specification, applicant uses the term "RNAi" to refer to both a compound and a process. As evidenced by Elbashir et al., RNAi is considered to refer to a process of sequence-specific gene silencing initiated by dsRNA that is homologous in sequence to the silenced gene, whereas the dsRNA or siRNA duplexes are considered to be the molecules that mediate the process of RNAi (see page 494). The acronym "RNAi" stands for RNA interference, which further reinforces the concept of RNAi as a process. Typically siRNAs are considered to be the effector molecule of the RNAi process. It appears that siRNA molecules are the compounds that may be intended to be instantly claimed. Clarification is required. Should applicants believe there is support in the art or the instant specification for RNAi as a compound, applicant is encouraged to cite this art in their response. In either case, for purposes of the instant search and examination the compounds RNAi and siRNA are interpreted broadly

as any RNA compound that is capable of interfering with the function of an mRNA transcript.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 1, 18, 20, and 28 are rejected under 35 U.S.C. 102(a) as being anticipated by Yu et al.

The instant invention is drawn to a polynucleotide comprising a nucleotide sequence encoding an RNAi operatively linked to a tissue specific promoter, a cell specific promoter, and/or an inducible promoter. The invention is further drawn to a vector, host cell, or pharmaceutical composition comprising the polynucleotide, wherein the pharmaceutical composition further comprises an excipient.

Yu et al. teach 21-nt siRNA duplexes that efficiently inhibit gene expression by RNAi when introduced into mammalian cells (see abstract). Yu et al. synthesized siRNAs within mammalian cells by using an expression vector. Yu et al. observed inhibition by the transcribed siRNAs and hairpin siRNAs by transfection into mouse host

cells. Yu et al. used an expression vector with a mouse U6 promoter. Yu et al. teach a composition comprising a siRNA and a cationic lipid, Lipofectamine.

Therefore, the instant invention is anticipated by Yu et al.

Claims 1, 18, 20, and 28 are rejected under 35 U.S.C. 102(e) as being anticipated by Engelke et al. (US 2003/0148519).

The instant invention is drawn to a polynucleotide comprising a nucleotide sequence encoding an RNAi operatively linked to a tissue specific promoter, a cell specific promoter, and/or an inducible promoter. The invention is further drawn to a vector, host cell, or pharmaceutical composition comprising the polynucleotide, wherein the pharmaceutical composition further comprises an excipient.

Engelke et al. teach a polynucleotide expression cassette encoding a siRNA which is operatively linked to a promoter to direct synthesis. Engelke et al. teach expression vectors and host cells comprising a nucleotide sequence encoding a siRNA (see page 20, for example). Engelke et al. teach pharmaceutical compositions and excipients (see page 28).

Therefore, the instant invention is anticipated by Engelke et al.

Claims 1 and 28 are rejected under 35 U.S.C. 102(e) as being anticipated by Fire et al. (US 6,506,559 B1).

The instant invention is drawn to a polynucleotide comprising a nucleotide sequence encoding an RNAi operatively linked to a tissue specific promoter, a cell

specific promoter, and/or an inducible promoter. The invention is further drawn to a pharmaceutical composition comprising the polynucleotide, wherein the pharmaceutical composition further comprises an excipient.

Fire et al. teach the process of RNAi. Fire et al. teach that a regulatory region (promoter) may be used to transcribe the RNA strand or strands (see columns 8 and 9). Inhibition may be targeted by specific transcription in an organ, tissue, or cell type. Fire et al. teach the use and production of expression constructs. Fire et al. teach compositions comprising the nucleic acid and a solution, lipid-mediated carriers, or chemical-mediated carriers (see column 9).

Therefore, the instant invention is anticipated by Fire et al.

Claims 1, 18, 20, and 28 are rejected under 35 U.S.C. 102(e) as being anticipated by Graham (US 6,573,099 B2).

The instant invention is drawn to a polynucleotide comprising a nucleotide sequence encoding an RNAi operatively linked to a tissue specific promoter, a cell specific promoter, and/or an inducible promoter. The invention is further drawn to a vector, host cell, or pharmaceutical composition comprising the polynucleotide, wherein the pharmaceutical composition further comprises an excipient.

Graham teaches an isolated genetic construct which is capable of delaying, repressing, or otherwise reducing the expression of a target gene in an animal cell which is tranfected with said genetic construct, wherein said genetic construct comprises at least two copies of a structural gene sequence and each copy of said

structural gene sequence is separately placed under the control of a promoter which is operable in said cell, and wherein said structural gene sequence comprises a nucleotide sequence which is substantially identical to at least a region of said target gene, wherein at least one copy of said structural gene sequence is placed operably in the sense orientation under the control of an individual promoter sequence, and wherein at least one other copy of said structural gene sequence is placed operably in the antisense orientation under the control of another individual promoter sequence (see claim 4). Graham teaches genetic constructs comprising a synthetic gene inserted into a suitable vector which is capable of being maintained and/or replicated and/or expressed in the host cell into which it is introduced (see column 13). Graham teaches a composition comprising the genetic construct and a suitable carrier, such as a liposome (see column 13).

Therefore, the instant invention is anticipated by Graham.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1, 18, 20, and 28 are rejected under 35 U.S.C. 103(a) as being unpatentable over Elbashir et al, in view of Tuschl et al. (WO 02/44321) and Luo et al. (US 6,211,164 B1).

The instant invention is drawn to a polynucleotide comprising a nucleotide sequence encoding an RNAi operatively linked to a tissue specific promoter, a cell specific promoter, and/or an inducible promoter. The invention is further drawn to a vector, host cell, or pharmaceutical composition comprising the polynucleotide, wherein the pharmaceutical composition further comprises an excipient.

Elbashir et al. teach that siRNA duplexes mediate RNA interference in cultured mammalian cells. Elbashir et al. teach that RNAi is a process of sequence-specific gene silencing initiated by dsRNA that is homologous in sequence to the silenced gene.

Elbashir et al. do not teach nucleotide sequences encoding a siRNA operatively linked to a promoter, or a vector or host cell comprising the nucleotide sequence. Elbashir et al. do not teach pharmaceutical compositions comprising the nucleotide sequence and an excipient.

Tuschl et al. teach that siRNAs represent a new alternative to antisense or ribozyme therapeutics.

Luo et al. teach antisense oligonucleotide mediated inhibition of human Chk1 gene expression. Luo et al. teach that antisense oligonucleotides may be introduced into a host cell through the use of one or more transfection reagents or vectors. The vectors comprise the sense or antisense cDNA as well as a promoter which is functional in a host cell and is able to elicit expression of the peptide or protein encoded by the nucleotide sequence. The promoter is operably linked to the nucleotide sequence (see column 5). Luo et al. teach pharmaceutical compositions comprising carriers, adjuvants or pharmaceutical vehicles (see column 6).

It would have been obvious to one of ordinary skill in the art to design a siRNA to inhibit the expression of a target gene as taught by Elbashir et al. Further, it would have been obvious to one of ordinary skill in the art to utilize a nucleotide sequence encoding a siRNA operatively linked to a promoter, as well as a vector or host cell comprising the nucleotide sequence, because Luo et al. teach that nucleotide sequences operatively linked to a promoter, as well as vectors and host cells comprising them, are suitable means for introducing nucleic acid sequences such as antisense oligonucleotides into host cells. Since both siRNAs and antisense oligonucleotides are sequence specific mediators of inhibition of target gene expression, one would be motivated to deliver either of these molecules into a cell by these means. As evidenced by Tuschl et al., siRNAs represent a new alternative to antisense or ribozyme therapeutics. One would have been motivated to create such compounds since Elbashir et al. teach that siRNA duplexes are efficient mediators of inhibition of target gene expression via RNAi and Luo et al. teach effective delivery of antisense oligonucleotides, which are also sequence specific mediators of inhibition of target gene expression, via operatively linking a promoter to a nucleotide sequence encoding the oligonucleotide, as well as teach using vectors and host cells. One would have been motivated to incorporate such compounds into a pharmaceutical composition comprising an excipient since such pharmaceutical excipients were known in the art at the time the invention was made to be beneficial for the delivery of oligonucleotides, as evidenced by Luo et al.

Finally, one would have a reasonable expectation of success given that Elbashir et al. teach designing siRNA molecules to direct cleavage of known genes and Luo et

al. teach operatively linked promoters, as well as vectors, host cells, and pharmaceutical compositions, each of which were known in the art to be components of a delivery system for oligonucleotides. One would reasonably expect that such a delivery system would not be confined to the delivery of antisense oligonucleotides, but would also benefit other sequence specific mediators of target gene expression, such as siRNA molecules.

Thus in the absence of evidence to the contrary, the invention as a whole would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Amy H. Bowman whose telephone number is 571-272-0755.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew Wang can be reached on 571-272-0811. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image

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For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

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Examiner
Art Unit 1635

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PATENT EXAMINER